

What is Claimed is:

1. An isolated and purified growth factor comprising an artemin amino acid sequence or a conservatively substituted variant thereof or a fragment thereof of at least 8 contiguous amino acids.

2. The isolated and purified growth factor of claim 1 which promotes survival of trigeminal ganglion neurons, nodose ganglion neurons, superior cervical ganglion neurons, and tyrosine-hydroxylase-expressing dopaminergic ventral midbrain neurons.

3. The isolated and purified growth factor of claim 1 comprising a mammalian sequence which is at least 75% identical to SEQ ID NO:19, SEQ ID NO:33 or a conservatively substituted variant thereof.

4. The isolated and purified growth factor of claim 3 comprising a human polypeptide sequence as set forth in SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO:5.

5. The isolated and purified growth factor of claim 4 comprising a human pro-artemin as set forth in SEQ ID NO:40 or a human pre-pro-artemin as set forth in SEQ ID NO:26 or SEQ ID NO:32 or a conservatively substituted variant thereof or a polypeptide comprising a non-artemin pre-pro- region and the human polypeptide sequence.

6. The isolated and purified growth factor of claim 3 comprising a mouse polypeptide sequence as set forth in SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36 or a conservatively substituted variant thereof.

7. The isolated and purified growth factor of claim 6 comprising a mouse pro-artemin as set forth in SEQ ID NO:41 or a mouse pre-pro-artemin as set forth in SEQ ID NO:27 or a conservatively substituted variant thereof or a polypeptide comprising a non-artemin pre-pro- region and the mouse polypeptide.

8. The isolated and purified growth factor of claim 1 comprising an amino acid sequence identical to the artemin polypeptide encoded by the human cDNA contained in the DNA deposited with ATCC on December 22, 1998.

9. The isolated and purified growth factor of claim 1 comprising an artemin polypeptide produced by a process comprising the steps of:

(a) transforming a host cell with human artemin cDNA clone deposited with ATCC on December 22, 1998 operably linked to expression regulatory elements  
5 and

(b) expressing artemin polypeptide encoded by the clone.

10. An isolated and purified polypeptide comprising:

(a) a pre- region of human artemin as set forth in SEQ ID NO:48 or a pre-region of mouse artemin as set forth in SEQ ID NO:49,

(b) a pro- region of human artemin as set forth in SEQ ID NO:50 or a pro-  
5 region of mouse artemin as set forth in SEQ ID NO:51,

(c) a pre-pro- region of human artemin as set forth in SEQ ID NO:52 or a pre-pro- region of mouse artemin as set forth in SEQ ID NO:53, or

(d) a conservatively substituted variant of (a), (b) or (c)..

11. A pan-growth factor comprising the artemin polypeptide fragment of claim 1 and a fragment of at least one other growth factor from the TGF- $\beta$  superfamily.

12. A nucleic acid comprising a polynucleotide encoding the pan-growth factor of claim 11.

13. A composition comprising the growth factor of claim 1 and a GFR $\alpha$  polypeptide.

14. The composition of claim 13 wherein the GFR $\alpha$  polypeptide is a GFR $\alpha$ 3 polypeptide or a GFR $\alpha$ 1 polypeptide.

15. An isolated and purified nucleic acid molecule or nucleic acid molecule complementary thereto comprising a nucleotide sequence encoding a growth factor of claim 1 or a fragment of said nucleotide sequence consisting of at least 15 contiguous nucleotides.

16. The isolated and purified nucleic acid molecule or nucleic acid molecule complementary thereto of claim 15 comprising a nucleotide sequence encoding an artemin polypeptide which promotes survival of trigeminal ganglion neurons, nodose ganglion neurons, superior cervical ganglion neurons, and tyrosine-hydroxylase-expressing dopaminergic ventral midbrain neurons wherein said nucleic acid molecule specifically hybridizes to a mature human artemin nucleotide sequence as set forth in SEQ ID NO:6, SEQ ID NO:7 or SEQ ID NO:8 or to a mature mouse artemin nucleotide sequence as set forth in SEQ ID NO:37, SEQ ID NO:38 or SEQ ID NO:39.

17. The isolated and purified nucleic acid molecule or nucleic acid molecule complementary thereto of claim 16 comprising a nucleotide sequence encoding an artemin polypeptide as set forth in SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:34, SEQ ID NO:35 or SEQ ID NO:36.

18. The isolated and purified nucleic acid molecule or nucleic acid molecule complementary thereto of claim 17 comprising a nucleotide sequence as set forth in SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39 or SEQ ID NO:44.

19. A vector comprising expression regulatory elements operably linked to the nucleic acid molecule of claim 15.

20. A host cell transformed with the vector of claim 19.

21. The isolated and purified nucleic acid molecule of claim 15 comprising

ATCC deposit made on December 22, 1998.

22. A host cell transformed with the vector of claim 21.

23. The isolated and purified nucleic acid molecule of claim 15 comprising a polynucleotide encoding a polypeptide selected from the group consisting of a human pro-artemin as set forth in SEQ ID NO:41, a human pre-pro artemin as set forth in SEQ ID NO:26 or SEQ ID NO:32, a mouse pro-artemin as set forth in SEQ ID NO:42, a mouse pre-pro-artemin as set forth in SEQ ID NO:29 and a polypeptide comprising a non-artemin pre-pro- region sequence and a human or mouse mature artemin amino acid sequence.

24. The isolated and purified nucleic acid molecule of claim 23 comprising a human pro-artemin nucleotide as set forth in SEQ ID NO:42, a human pre-pro-artemin nucleotide as set forth in SEQ ID NO:24, SEQ ID NO:30 or SEQ ID NO:44, a mouse pro-artemin nucleotide as set forth in SEQ ID NO:43, or a mouse pre-pro-artemin nucleotide as set forth in SEQ ID NO:27.

25. A recombinant nucleic acid molecule comprising an artemin nucleotide sequence or complement thereto wherein the artemin nucleotide sequence encodes an amino acid sequence selected from the group consisting of a pre-pro-artemin polypeptide, a pro-artemin polypeptide, a mature artemin polypeptide, a conservatively substituted variant thereof and a fragment thereof having at least 8 contiguous amino acids.

26. The isolated and purified polynucleotide of claim 15 which is an artemin antisense oligonucleotide.

27. An isolated and purified nucleic acid molecule comprising a polynucleotide encoding:

(a) a pre- region of artemin as set forth in SEQ ID NO:54 or SEQ ID NO:55;

(b) a pro- region of artemin as set forth in SEQ ID NO:56 or SEQ ID NO:57;

(c) a pre-pro- region of artemin as set forth in SEQ ID NO:58 or SEQ ID NO:59; or

(d) a conservatively substituted variant of (a), (b) or (c).

28. An isolated and purified antibody which specifically reacts with the artemin polypeptide or fragment of claim 1.

29. A method for detecting expression of an artemin polypeptide in a sample comprising contacting the sample with an antibody according to claim 28 and detecting binding of the antibody to the artemin polypeptide.

30. A method for detecting expression of an artemin mRNA in a sample which comprises detecting a polynucleotide in the sample that specifically hybridizes to a polynucleotide consisting of SEQ ID NO:9.

31. The method of claim 30, wherein detecting the polynucleotide comprises:

(a) contacting mRNA of the sample with a polynucleotide that specifically hybridizes to a polynucleotide consisting of SEQ ID NO:6; and

(b) detecting the existence of a hybridization complex between the polynucleotide and the artemin mRNA.

32. The method of claim 30, wherein the detecting step comprises:

(a) producing a cDNA from the artemin mRNA using the reverse transcription method;

(b) contacting the cDNA with at least two oligonucleotides that specifically hybridize to the cDNA to define a region of the cDNA to be amplified;

(c) amplifying the cDNA region; and

(d) detecting the amplified cDNA region.

33. A method for providing trophic support to and/or for producing differentiation of a cell comprising treating the cell with an effective amount of an artemin polypeptide or fragment thereof.

34. The method of claim 33, wherein the treating step comprises administering to the cell the artemin polypeptide or fragment with or without a GFR $\alpha$ 3 polypeptide.

35. The method of claim 33, wherein the target cell is within a patient and the treating step comprises administering to the patient the artemin polypeptide or fragment with or without a GFR $\alpha$ 3 polypeptide.

36. The method of claim 33, wherein the target cell is within a patient and the treating step comprises administering to the patient a polynucleotide encoding the artemin polypeptide or fragment.

37. The method of claim 33, wherein the artemin polypeptide is expressed by a cell implanted into the patient.

38. The method of claim 33, wherein the target cell is a neuron in a patient suffering from peripheral neuropathy, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, ischemic stroke, acute brain injury, acute spinal chord injury, a nervous system tumor such as neuroblastomas, multiple  
5 sclerosis, infection or an enteric disease such as idiopathic constipation or constipation associated with Parkinson's disease, spinal cord injury or use of opiate pain-killers or the target cell is a non-neuronal cell in a patient suffering from small cell lung carcinoma.

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